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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/734,847	12/12/2000	C. Frank Bennett	ISPH-0524	4732

26259 7590 10/17/2003

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EXAMINER	
EPPS FORD, JANET L	

ART UNIT	PAPER NUMBER
1635	18

DATE MAILED: 10/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/734,847	BENNETT ET AL.	
	Examiner	Art Unit	
	Janet L. Epps-Ford, Ph.D.	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 August 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-16 and 31-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-16 and 31-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments

Claim Rejections - 35 USC § 102

2. Claims 1-2, 6-13, and 31-32 remain rejected under 35 U.S.C. 102(b) as being anticipated by Kole et al. (WO94/26887-A1) for the reasons of record set forth in the Official Action mailed 3-05-03.

3. Applicants traverse the instant rejection on the grounds that the teachings of Kole et al. that comprises the use of antisense oligonucleotides to alter aberrant splicing is not the same as the present invention, which teaches modulation of native mRNA processing in a cell such that the response of that cells to a stimulus is altered. Applicants refer to claim 1 and Examples 6-18 of the specification as filed to support their arguments, see page 14 of response filed 8-01-03. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., wherein the claimed method recites a method of modulation of native mRNA processing in a cell such that the response of that cells to a stimulus is altered) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Moreover, as stated in the prior Office Action, the antisense oligonucleotides of Kole et al. may be designed to block a mutated element, a cryptic element, or ***a native element*** such as a 5' splice site, a 3' splice site (which correspond to an intron-exon borders), or a branch point

(page 8, lines 5-10). The methods of Kole et al. are disclosed as being useful for targeting human pre-mRNA encoding beta-, and alpha-globin, beta-hexoseaminidase, phenylalanine hydroxylase, and cystic fibrosis gene premRNA (which is known in the art to encode a membrane protein; see bridging paragraph pages 10-11). Additionally, the antisense oligonucleotides of Kole et al. may contain at least one, or all methyl phosphonates, methyl phosphonothioates, phosphoromorpholidates, phosphoropiperazidates, and phosphoramidates, and may contain a nucleotide having a lower alkyl substituent at the 2' position thereof (page 9, lines 4-26). In regards to the modulation of splicing that results in an altered ratio of splice products, and exclusion of one or more exons from the mature mRNA see

Double Patenting

4. Claims 1, 2, 4-16 and 31-33 remain rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-31 of U.S. Patent No. 6,210,892 for the reasons of record set forth in the prior Office Action.

Applicants traverse the instant rejection on the grounds that the current claims as amended are no longer obvious over the cited patent and withdrawal of the rejection is respectfully requested. Contrary to Applicant's assertions, to the extent that the instant claims recite wherein the method comprises binding to the target wild-type mRNA an antisense compound having at least one 2'aminooxy, or wherein the compound is a peptide nucleic acid having at least one lysine residue at it's C-terminus, it remains that the current claims are obvious over the issued US Patent.

As stated in the prior Office Action the issued claims are limited to methods comprising the use of antisense oligonucleotides comprising at least one 2'-methoxyethoxy, 2'-

dimethylaminooxyethoxy, 2'-dimethylaminoethoxyethoxy, 2'-acetamide, morpholino, or peptide nucleic acid modification. It is noted that absent evidence to the contrary, a 2'-dimethylaminooxyethoxy modification comprises the 2'-aminooxy modification recited in the currently amended claims.

Additionally, in regards to instant the claims which recite peptide nucleic acid having a lysine residue at its C-terminus or peptide nucleic acid having an arginine residue at its C-terminus, these claims are an obvious variation of claims 1-31 of the issued US Patent since oligonucleotides modified with a polylysine group since this modification is disclosed in the specification of the US Patent (col. 23, lines 37-44) as enhancing cellular uptake of oligonucleotides at the cellular level. Moreover, one having ordinary skill in the art would have been motivated to do this because these embodiments are disclosed as being a preferred embodiment in the issued US Patent.

Therefore, it remains that the invention as a whole is *prima facie* obvious over Bennett et al. (US Patent 6,210,892).

Conclusion

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford, Ph.D. whose telephone number is 703-308-8883. The examiner can normally be reached on Monday-Thursday, 8:30 AM - 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on 703-308-0447. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Janet L. Epps-Ford, Ph.D.
Examiner
Art Unit 1635

JLE

SEAN McGARRY
PRIMARY EXAMINER